REMARKS

Claims 1-20 are pending in this Application. Claims 1 and 12 are written in independent form. By this Amendment, claims 1 and 12 are amended. Support for the amendments may be found at least at paragraphs [0001] and [0003] of the published Specification. Thus, no new matter is added.

Specification

The title of the specification is objected to for failing to be descriptive. The title of the specification is amended. As such, withdrawal of the objection is requested.

Claim Rejections Under 35 USC §101

Claim 1 is rejected under 35 USC §101 for failing the 'machine or transformation' (T&M) test set forth in *In re Bilski*. However, according to the US Supreme Court, there ar four independent categories of invention under 35 USC §101 including <u>processes</u>, machines, manufactures and compositions of matter. The Court also indicated that the T&M test is not the sole test for patent-eligibility under 35 USC §101. Moreover, according to the recent guidelines from the USPTO issued on June 28, 2010 regarding examination of claims for compliance with 35 USC §101, Examiners may reject claims using the T&M test that are drawn to an abstract idea. In the present case, there is no allegation that the claim 1 is drawn to an abstract idea. Rather, it is merely alleged that 'the claim lacks either 1) being tied to another statutory class (such as a particular apparatus) or 2) transforming underlying subject matter to a different state or thing (In re Bilski)'. As such a proper rejection under 35 USC §101 has not been established.

Although proper grounds for rejection have not been established, claim 1 is amended address the rejection.

Claim 12 is rejected for allegedly being readable on non-statutory subject matter. Claim 12 is amended in the manner proposed by the Examiner. As such, it is understood that claim 12, and its dependent claims are statutory subject matter and comply with 35 USC §101.

Example Embodiment of the Claimed Subject Matter

The subject matter described in the present claims relates to a method of iterative sampling that relies on weighting factors. In an embodiment, the process enables identifying in each iteration, the parts of a sampling space that were comparatively little sampled so far and that need to be sampled further to improve the precision of desired estimates. The weighting factors are not an approximation to an optimal function and may vary from iteration to iteration. The weight of points within the region into which sampling was concentrated will get reduced, and sampling in the next iteration will be concetrated in other regions. Thus, the focus of the sampling function will move around in subsequent iterations. For example, Fig. 4 shows weighting factors $\rho_{i,t}$ (circles) that have different values in different state areas of the system (discontinuous line). In a further iteration, the weighting factors $\rho_{i,\,t}$ would again be different.

Claim Rejections Under 35 USC §102

Claims 1-20 are rejected under 35 USC §102(b) as being anticipated by "Multidimensional Adaptive Umbrella Sampling: Applications to Main Chain and Side

Chain Peptide Conformations" to Bartels (hereinafter "Bartels"). The rejection is repsectfully traversed.

The difference between Bartels "Adaptive Umbrella Sampling" and the claimed "Incremental Umbrella Sampling" is deescribed, for example, in paragraphs [0022] and [0023] of the published specification of the present application.

In Bartels, a particular sampling potential $\rho°0$ is sought to be optimized, where the sampling potential is defined prior to starting simulations, e.g., Eqs. 1 and 2 of Bartels. The sampling potentials ρ_i () in subsequent iterations converge to a particular sampling potential ρ_{opt} (). Thus, Bartels describes determining potentials that <u>converge to a particular preselected sampling potential</u>. As such, Bartels cannot disclose a third step determining weighting factors $\tilde{\rho}_{i,t}$ for states $x_{i,t}$ generated so far by using sampling distribution functions $\rho_i(x)$ determined so far and a fitting step for determining a sampling distribution function $\rho_j(x)$ for the next iteration by fitting $\rho_j(x)$ to $\tilde{\rho}_{i,t}O(x_{i,t})$ for states $x_{i,t}$ generated so far, wherein $O(x_{i,t})$ is a function, respectively a property, of the states $x_{i,t}$, as claimed.

In rejecting the claims, it is alleged that Bartels discloses an iteration procedure that includes a third step determining weighting factors $\tilde{\rho}_{i,t}$ for states $x_{i,t}$ generated so far by using sampling distribution functions $\rho_i(x)$ determined so far and a fitting step for determining a sampling distribution function $\rho_j(x)$ for the next iteration by fitting $\rho_j(x)$ to $\tilde{\rho}_{i,t}O(x_{i,t})$ for states $x_{i,t}$ generated so far, wherein $O(x_{i,t})$ is a function, respectively a property, of the states $x_{i,t}$.

In Bartels, the analysis step is performed to estimate $\tilde{p}kl...$, i.e., a discretionized version of the marginal probablity density of selected degrees of freedom $k, l ...$. The

analysis partitions the conformational space into bins based on the selected degrees of freedom, counts the number of times $n_{i,kl}$ each bin gets sampled in the different iterations of i, and uses the counts in the estimation process (see Eqs. 7 and 8 of Bartels).

In contrast to Bartels, the rejected claims recite that the analysis is done to determine weighting factors $\tilde{\rho}_{i,t}$ for states $x_{i,t}$. This estimation procedure does not depend on partitioning the conformational space into bins as described in Bartels.

Further, the estimate $\tilde{p}kl...$ of the discretionized version of the marginal probablity density function in Bartels are related to weighting factors by Equation 18 of Bartels (page 1455), where K ($x_{i,t}$) and L ($x_{i,t}$) denote the index of the first and second degrees of freedom, respectively (see Equation 17 of Bartels). In contrast to the weighting factors of the claimed invention, in Bartels the estimate for a particular bin kl does not depend on whether comparatively few or many states have been sampled in this bin. If few states have been sampled, their associated weights are comparatively large. If many states have been sampled, their associated weights are comparatively small (see paragarphs [0022] and [0052] of the published application). Therefore, the estimate of the marginal probability density function disclosed in Bartels cannot be used to distinguish regions that have been sampled abundantly from regions that have been sampled comparatively few times. As such, Bartels cannot disclose or suggest the claimed "third step" of determining weighting factors $\tilde{\rho}_{i,t}$ for states $x_{i,t}$ generated so far by using sampling distribution functions $\rho_i(x)$ determined so far.

As discussed above, in Bartels the sampling potential is determined by fitting to a discretionized version of the marginal probability density function (see page 1452 of

Bartels). In contrast, the sampling potential in the pending claims is determined to fit to the product $\tilde{p}_{i,t}O(x_{i,t})$. As also discussed above, the present claims relate to distinguishing between regions of the conformational space that are sampled comparatively few times (e.g., few points with high weights) and parts that have been sampled abundantly and contain many points with small weights. As Bartels does not distinguish between these two situations, Bartels cannot anticipate the pending claims. For example, using the method of Bartels, if in two successive runs a particular region is comparatively abundantly sampled or not <u>will not change the sampling potential</u>. In contrast, the claimed method will bias sampling towards or away from this regions, respectively. As such, Bartels cannot anticipate steps 4 and 5 of the present claims.

Because Bartels does not and cannot disclose all of the features recited in the rejected claims, withdrawal of the rejection is requested.

CONCLUSION

Accordingly, in view of the above amendments and remarks, an early indication of the allowability of each of claims 1-20 in connection with the present application is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact John W. Fitzpatrick at the telephone number of the undersigned below.

Pursuant to 37 CFR §§ 1.17 and 1.136(a), Applicants petition for a one (1) month extension of time for filing a reply to the March 26, 2010 Office Action, and submit the required $65.00 extension fee herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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